

Comments from the United States
Revised draft risk profile: Dechlorane Plus
UNEP/POPS/POPRC.16/CRP.2

Production, Use, and Regulatory Status

- The draft risk profile states in paragraph 25 that “certain restrictions, approval and notification requirements for imports and use are also in place in the United States, New Zealand and Thailand.” We suggest the following edits be made to this sentence: “certain restrictions, approval, reporting, and/or notification requirements for production, imports, and/or use.”
- The draft risk profile notes in paragraph 31 that uses of Dechlorane Plus in the EU include uses in formulations or re-packing, at industrial sites and by professional users “as well as consumer uses of Dechlorane Plus when contained in articles.” We think it would be more accurate to say, “Dechlorane Plus is also contained in some articles used by consumers.”
- We also note that since Table 3 in INF 14 pertains to national regulatory processes, information listed in Table 3 about the activities of the International Chemical Secretariat should be included in a different section or the title of the table should be changed.

Bioaccumulation

- We wonder why BCFs were included as evidence of bioaccumulation when paragraph 54 acknowledges that “aqueous exposure is expected to be of limited importance in terms of bioaccumulation potential”. We suggest a clarification be added to the draft risk profile that this information is not the basis of the conclusion on bioaccumulation.
- The draft risk profile states in paragraph 63 that field monitoring data suggest that Dechlorane Plus is bioavailable and can exceed levels in biota that are of concern based on critical body burden considerations related to baseline narcosis. However, just being present/available does not create an expectation for toxicity. We do not think this is relevant to the bioaccumulation section.

Exposure

- Regarding the sentence in paragraph 100 that states “the input of Dechlorane Plus to the environment in [the Great Lakes] area is continuing, presumably because its use and production are not regulated.” As noted in Table 3 of POPRC.INF/14, Dechlorane Plus is subject to reporting requirements in the United States under TSCA. In addition, the draft risk profile notes in paragraph 26 that production at the manufacturing facility in Niagara Falls, New York ceased in 2016. We suggest that the sentence be deleted.

Hazard Assessment for Endpoints of Concern

- Paragraph 113 states that “No acute toxicity was observed in the freshwater protozoan, *T. thermophila*, but significant increase in DNA damage was observed at DP concentrations from 300 to 1500 µg/L after 30 minutes exposure (Dou et al., 2015).” However, Dou et al.

resuspended the protozoa in Tris buffer, then added the test substance in distilled water and 0.5% DMSO. We question the relevance of this finding. As noted in paragraph 111, Dechlorane Plus will partition to particulate matter in aquatic environments, which will limit uptake, but the test system was devoid of particulate matter. Further, no increase in DNA damage was observed at 60,000 ng/L, which is far above the water solubility of DP (i.e., <44 ng/L).

- There were multiple instances where there were cursory reviews of studies on endpoints like oxidative stress and speculations about how they “could have an impact”, “may lead to”, or “may contribute to” the development of adverse effects (see, e.g., paragraphs 114 and 136 and Table 3, bullet 4 under adverse effects).
- The draft risk profile states that for the first study described in paragraph 114 no clear dose-response was observed. This means there is not a causal relationship.
- Also in paragraph 114, the draft risk profile states that increased micronuclei formation was observed only for highest dose (100 µg/L) tested (Barón et al., 2016). We wonder what linkage there is, causally, between micronuclei formation and an adverse effect in the species. Is this an adaptive response?
- Paragraph 115 lists negative studies and one positive study, but there is no discussion about data quality, reliability, or relevance. We did note that the negative studies were published in peer-reviewed journals, and the one positive study was from a meeting proceeding, but the link was not working so we were unable to review the cited source.
- Paragraph 117 cites to a study where Dechlorane Plus was reported to cause effects on “neurobehavioral abnormalities, axonal growth reduction, apoptotic markers in muscle and brain Ca^{2+} homeostasis (Chen et al., 2019).” However, Chen et al. (2019) did not provide information about the test media (e.g., total organic carbon (TOC) content), rather they only stated the salinity of the water. This is an important consideration given that the draft risk profile states in several places that Dechlorane Plus will adsorb to particulate matter. If particulate matter/TOC was intentionally removed from the test system, then how are these findings relevant to real world exposures?
- In the study described in paragraph 121, there is no description of the physiological or functional effects or adverse outcome. The effects described were on the generalized stress response, small G-protein signal cascades, Ca^{2+} signalling pathway and metabolic process, and induced apoptosis in the liver.
- The draft risk profile describes a study in paragraph 122 where adult zebrafish received 3 µg/g by gavage twice in a 6-day study, with increased catalase activity observed in the liver indicating an oxidative stress response. This seems like a very stressful way to dose such a small fish, perhaps inducing oxidative stress.
- The discussion in paragraph 123 of maternal uptake and transfer in fish and frogs and Dechlorane Plus found in developing embryos of female sharks is about exposure, not effects.
- In paragraph 124, about potential neurotoxic effects in earthworms, the linkage between the biochemical changes and an adverse effect is not established.
- We note that paragraph 131 states that acute toxicity studies in experimental animals suggest low concern for acute toxicity via the oral, inhalation and dermal routes of exposure. No

adverse health effects were observed in any of the identified repeated-dose oral toxicity studies, testing dose levels up to 5000 mg/kg bw. The draft risk profile points out that this is an extremely high dose (5 times the limit dose of the OECD test guideline).

- Paragraph 132 discusses liver impairments in mice at high-dose exposure. The draft risk profile states that relative liver weight was significantly increased in the 2000 mg/kg group. Oxidative stress to the liver was shown by significant increase in SOD activity and the oxidative DNA-damage marker 8OHdG at all doses, as well as increased catalase (CAT) activity at 2000 mg/kg. We question the relevance of these results to determining if there are adverse effects.
- Paragraph 133 describes a 90-day oral study with rats and stated that no significant changes in absolute body or liver weight or liver histopathology were observed. These are common measures of effects in toxicity tests, which indicates there are no adverse effects/outcomes due to exposures in this study.
- In paragraph 134 the draft risk profile notes that in a 13-week oral feeding study in rats, absolute and relative liver weight increased, but no associated histopathology was observed. This is adaptive, more than likely enzyme induction.
- The draft risk profile also states in paragraph 134 that effects on lung tissues were observed as increased number of macrophages in alveoli, and significant increase in absolute lung weight was observed. This seems like an effect on clearance, as it relates to lung overload in rats.
- For human toxicity, as noted above, the available acute studies indicate a low hazard concern, and the available repeated dose studies indicate low/moderate hazard concerns. However, the draft document relies on “altered glucose metabolism and lipid tissue in mice” as supporting information for adverse effects because these effects “*may* contribute to development of type-2 diabetes” (paragraph 136).